

Decision Support Information System for Hardly Diagnosing Diseases

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Abstract

The paper describes research and development of mathematical based software diagnostic service and applied interfaces for it, which together presents medical decision support information system. First implementation in diagnosis of children hypermobility syndrome proposed. This work was carried out by IT-park of PetrSU in the collaboration with Department of Pediatrics. The diagnostic service uses innovative mathematical method named diagnostic iteration model. This model is abstract and can be applied in diagnosis of large number of diseases, diacrisis of which are not formalized and are held on the grounds of indirect signs and symptoms.

Index Terms: Mathematical methods of diagnostics, Statistics, Hypermobility syndrome.

I. INTRODUCTION

Currently, in medicine there are several diseases, diacrisis of which are not formalized and are held on the grounds of indirect signs and symptoms. They are, in particular, hypermobility syndrome and such neurological diseases as Alzheimer, Parkinson's syndrome, and others. As a consequence, only specialized experts can diagnose these diseases and conditions with a reasonable certainty. This situation has serious implications when diagnosing children's hypermobility syndrome, as identification of the degree of this disease is important not only to assess general health of the child, but also to prevent possible secondary diseases. Hypermobility syndrome is disease affecting cardiovascular, nervous and other systems of the child body; therefore, a pediatrician who does not have special diagnostic tools, treats secondary diseases without noticing initial pathology. As a result, the child has a large number of secondary diseases, but does not receive the necessary treatment until he is examined by experts who can diagnose hypermobility syndrome [1].

It is obvious that the expert is not able to check and diagnose all potential patients, and a tool that will allow doctors without highly specialized training to make diagnosis is really needed. As implementation of such a tool it is suggested to develop a decision support information system – electronic medical assistant. Such information system should rely on mathematical methods of diagnosis, be able to come to conclusion on the most likely diagnosis for the patient based on the available statistical data. What is meant is supervised learning system, so it directly reflects specific subject area, where the expert makes a diagnosis based on his own experience and knowledge of relationships between symptoms and diseases. Obviously, classification of the diagnostic tool as a decision support system implies the possibility of a diagnostics based on a limited set of symptoms. Hence there is the second problem to be solved by diagnostic system – selection of medical tests for the accuracy of the diagnosis.

Diagnostic information system implements the concept of a diagnostic service, which has a variety of interfaces: web-interface for diagnostics and working with statistical database, an interface for mobile devices and plug-ins for integration into software systems of medical facilities. All interpretations of the diagnostic service interface are simple and intuitive to operate, do not require any specific training; the results of their work are accompanied with detailed commentary. As a consequence, it expands market for the end product, as the diagnostic service can be used not only by health care professionals, but by preschool and school specialists as well as parents. Availability of different interfaces, ease of implementation, diagnostic quickness and the potential of its application to a large number of diseases provide wide circulation of the diagnostic service.

II. DEVELOPMENT OF DIAGNOSTIC SERVICE

A. Problem description

Suggested concept of diagnostic program development by inherent model corresponds to a large number of diseases and health properties of the organism, diagnosis of which is related to identification of indirect symptoms. But primarily, implementation of the diagnostic service aims to solve the problem of uncertainty in diagnosing such disease as children's hypermobility syndrome.

The term hypermobility syndrome (HS) combines a group of connective tissue diseases, which are caused by impaired development of connective tissue in the embryonic and postnatal periods [2, 5]. HS is the cause of many secondary diseases of the cardiovascular, nervous and other systems of the body, and without timely prevention it leads to serious consequences for the children health affecting their lives. At present, in the medical community they describe three degrees of children's HS [3]:

- First degree – it includes children with absent or faint hypermobility syndrome.
- Second degree – it includes children with pronounced HS, which, however, is not reflected in the structural change of the connective tissue and organ system diseases.
- Third degree – it includes children with pronounced hypermobility syndrome, which resulted in serious disturbances in the structure of the connective tissue and serious diseases of organs and body systems.

There are several methods of diagnosis of HS based on external symptoms, but given that they are focused on "manual" application, the number of used symptoms is small, and the diagnostic accuracy is insufficient. The use of computer technology allows increasing the number of analyzed symptoms to 138 and improving the accuracy of diagnosis. HS symptom set was compiled as a part of a joint study with the Department of Pediatrics of Petrozavodsk State University based on medical records of 1487 children. For the convenience the whole set of HS symptoms was divided into three groups, each of which is divided into smaller sub-groups:

- external phenotypic symptoms;
- phenotypic symptoms of the CNS (central nervous system), ANS (autonomic nervous system) and internals;
- ultrasonographic markers of children HS.

Pediatrics expert diagnosed each of the 1487 surveys on the basis of his own experience and knowledge. This data can be used in the future for training and testing the developed mathematical methods of diagnosis.

B. Specification of mathematical methods

The core of diagnostic service software implementation is a set of mathematical methods that come to diagnostic conclusion based on statistical relationships between latent signs of the disease and the final diagnosis. These methods also perform a selection of recommended medical tests to confirm the diagnosis. Mathematical description of the diagnostic model is formulated in general form, abstracted from the particular problem of diagnosing children hypermobility syndrome.

1) Formal statement of the problem

All subject area objects (patients) comprise a set Ω – that is a general set of objects. Part of the objects that have been diagnosed by experts comprise a teaching selection $\Omega^* \subset \Omega$. Each object X_i from the general set Ω is a m -dimensional vector of test results based on the set of symptoms M ($m = |M|$).

$$X_i = (x_{1i}, \dots, x_{mi})$$

Vector column that contains test result data based on the set of symptoms is called **medical record** of the patient (object). Test result x_{ij} can be either tangible x_{ij}^* (the object was tested) or empty \emptyset . Tangible test result x_{ij}^* is one of the finite sets of possible values of test result R_{ij} . Test result can be represented as:

$$x_{ij} = \begin{cases} x_{ij}^*, & \text{object } i \text{ was tested for symptom } j \\ \emptyset, & \text{object } i \text{ was not tested for symptom } j \end{cases} \quad (1)$$

As it was stated above, all teaching selection objects have been diagnosed by experts. Thus teaching selection Ω^* is divided into k number of non-overlapping subsets A_k based on index set of possible diseases S . Set A_k ($k \in S$) that contains objects with diseases k , is called « k class». Expression $X_i \in A_k$ means «object X_i has disease k ». Let $N = \sum_{k \in S} N_k$, where N_k is the number of objects in teaching selection that have disease k , N is the total number of objects in teaching selection.

When examining hidden dependencies of initial data in the teaching selection Ω^* it is necessary to build a **membership rule** Ψ , that will define the degree of a certain object X_0 membership in k ($k \in S$) class based on its medical test results.

$$\Psi(X_0, k) = \xi_k \quad (2)$$

Membership degree ξ_k corresponds to the probability that object X_0 belongs to the set A_k ($k \in S$), that means it possesses values at the interval $[0; 1]$.

It is also required to build a **decision rule** Φ to precisely assign object X_0 to one of the classes A_k ($k \in S$) based on object X_0 medical record and detected dependencies in the teaching selection Ω^* .

$$\Phi(X_0) = k^* \mid X_0 \in A_k \quad (3)$$

2) Diagnostic iteration model

Diagnostic service must solve two problems: diagnosing amphibolous diseases and selecting additional medical tests. The problems can be solved using single computerized diagnostic iteration model. The model is a step-wise diagnostic algorithm (see Fig. 1)

with actions being divided into two groups: (I) – actions done by a human being (diagnostic service user), (II) – actions done by computerized system.

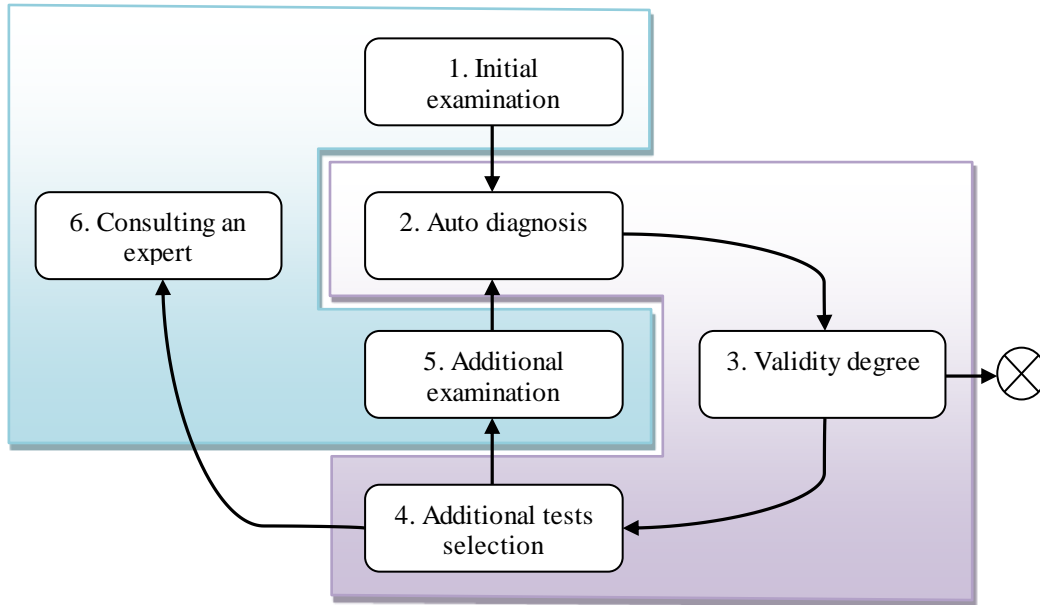


Fig. 1. Diagnostic iteration model

Iteration model can be technically presented in the form of the following algorithm:

- Step 1: Initial examination of object X^* in the test set $T_0 \subset T$, where T – is a set of all medical tests of the relevant disease.
- Step 2: Computerized disease diagnostics based on a set of test results T_i , where i – is the number of diagnostic cycle iteration (starting from 1).

$$T_i = T_0 + \bigcup_{j=1}^i T_j^*$$

Diagnostics result is a vector of membership rule values $\Psi_i(X^0, A_k) = \xi_k^i$ for each of the diagnostic classes $A_k \in S$, where S is a set of diagnostic classes:

$$(\xi_1^i, \xi_2^i, \dots, \xi_{|S|}^i)$$

At Step 2, apart from probabilistic distribution over diagnostic classes, computerized system makes a supposition assigning the object to one of the diagnostic classes using decision rule Φ .

- Step 3: Evidence degree evaluation of the diagnosis $\Theta_i(X_0)$ assigned at Step 2. If evidence degree is $\Theta_i(X_0) = 1$ and the subject of checkup is not interested in further clarification of the diagnosis, it is the end of the algorithm; otherwise go to Step 4.
- Step 4: Selection of additional tests based on a number of symptoms of set T_i^* implementation of which enables maximum clarification of the diagnosis. If the selection of additional tests is not possible, it is the end of the algorithm (the last diagnosis is considered to be certain, the system suggests consulting an expert); otherwise go to Step 5.
- Step 5: Checking object X^* with a set of additional tests T_i^* and then going to Step 2.

It is required to solve 3 particular independent subproblems to implement iteration model:

1. Finding diagnostic method based on incomplete checkup data.
2. Finding evidence degree evaluation method for the diagnosis based on incomplete checkup data.
3. Finding a method for selecting additional tests, which satisfy external limits in the best way, maximizing the accuracy of the follow-up diagnosis.

2.1) *Method of the sampling frequencies*

Method of sampling frequencies solves the problem of assigning a particular object to one of the diagnostic classes based on insufficient checkup data. This method is a modification of the frequency method [6], which is highly effective, but it cannot be used with insufficient checkup data. To build the membership rule for the method of sampling frequencies it is suggested using statistical regularities, detected based on teaching selection data.

Let A_k be a random event of class k object appearance. Event of getting result r for test j of particular object X_0 stands for B_j^r ($j \in M$). Let us suppose that at some moment in time i they know the results of a set of tests T_i . Then, to evaluate the membership of object X_0 in one of the diagnostic classes k it is required to evaluate conditional probability of event A_k taking place on the condition of event combination $B_1^{r_1}, \dots, B_t^{r_t}$ taking place, where $\{1, \dots, t\} = T_i$.

$$P(A_k | B_1^{r_1}, \dots, B_t^{r_t}) \tag{4}$$

Using Bayes formula to calculate the above stated probabilities the following correlation is obtained [9]:

$$P(A_k | B_1^{r_1}, \dots, B_t^{r_t}) = \frac{P(B_1^{r_1}, \dots, B_t^{r_t} | A_k) \cdot P(A_k)}{P(B_1^{r_1}, \dots, B_t^{r_t})} \tag{5}$$

Using total probability formula in denominator gives final correlation for calculating the probability of membership of a particular object X_0 in class A_k when the results of the set of tests are known:

$$P(A_k | B_1^{r_1}, \dots, B_t^{r_t}) = \frac{P(B_1^{r_1}, \dots, B_t^{r_t} | A_k) \cdot P(A_k)}{\sum_{h \in S} P(B_1^{r_1}, \dots, B_t^{r_t} | A_h) \cdot P(A_h)} = \Psi(X_0, k, T_i) \tag{6}$$

Correlation **Ошибка! Источник ссылки не найден.** is the membership rule $\Psi(X_0, k, T_i)$ of method of sampling frequencies. Decision rule Φ , assigning object to a specific diagnostic class, is based in the method of sampling frequencies on maximum a posterior probability:

$$\Phi(X_0) = \operatorname{argmax}_k \Psi(X_0, k, T_i) = \operatorname{argmax}_k P(A_k | B_1^{r_1}, \dots, B_t^{r_t}) \tag{7}$$

The main difficulty in using method of sampling frequencies is to find evaluations of probabilities involved in calculating the value of membership rule $\Psi(X_0, k, T_i)$. Probability $P(A_k)$ of class k object taking place can be estimated based on frequency of class k object in the teaching selection [7]:

$$P(A_k) = \frac{N_k}{N} \tag{8}$$

Evaluation of conditional probability $P(B_1^{r_1}, \dots, B_t^{r_t} | A_k)$ of getting the given set of test results $(B_1^{r_1}, \dots, B_t^{r_t})$ on the condition that object X_0 belongs to class k is calculated as:

$$P(B_1^{r_1}, \dots, B_t^{r_t} | A_k) = \frac{P(B_1^{r_1}, \dots, B_t^{r_t}, A_k)}{P(A_k)} \quad (9)$$

$$= \frac{P(B_1^{r_1} | B_2^{r_2}, \dots, B_t^{r_t}, A_k) \cdot P(B_2^{r_2} | B_3^{r_3}, \dots, B_t^{r_t}, A_k) \cdot \dots \cdot P(B_t^{r_t} | A_k) \cdot P(A_k)}{P(A_k)}$$

Evaluation of probability $P(B_1^{r_1}, \dots, B_t^{r_t} | A_k)$ using the above stated formula is resource intensive and it is required to collect a huge amount of teaching selections. Thus, the formula cannot be used. On the other hand, as some dependencies between initial diagnostic symptoms in the teaching selection are negligibly small, formula can be significantly simplified. For that purpose it is required to build a *network of dependencies* of diagnostic symptoms [8]. The network of dependencies is a weighted unoriented graph, the nodes of which correspond to disease symptoms and edges show the dependency of two symptoms the nodes of which they connect. Edge weight shows the value of dependency between the corresponding symptoms. When building the network of dependencies the edges with light weight are neglected; thus, the final network of symptom dependencies will show the strongest connections. Using data of the network of symptom dependencies formula (9) can be written as:

$$P(B_1^{r_1}, \dots, B_t^{r_t} | A_k) = P(B_1^{r_1} | G_1^{R_1}, A_k) \cdot P(B_2^{r_2} | G_2^{R_2}, A_k) \cdot \dots \cdot P(B_t^{r_t} | A_k) \quad (10)$$

where $G_j^{R_j}$ is a set of events when symptoms arc-connected with symptom j in the network of dependences take values from the set R_j .

To evaluate multipliers in the right part sample frequencies will be used, in particular:

$$P(B_j^{r_j} | A_k) = \frac{N_k \langle X_i | x_{ij} = r_j \rangle}{N_k} \quad (11)$$

where $N_k \langle X_i | x_{ij} = r_j \rangle$ is the number of objects in diagnostic class k whose symptom j takes the value r_j ($x_{ij} = r_j$);

N_k is the number of objects in diagnostic class k .

2.2) Method of additive validity

General idea of measuring validity degree of computerized diagnosis is to define the test results that comprise the basis for expert's conclusion, which set of tests is sufficient and which is not. For each medical test j of the teaching selection the value vector of *validity coefficients* of test results $j - \bar{K}_j$ is calculated.

$$\bar{K}_j = (k_j^1, \dots, k_j^r) \quad (12)$$

Validity coefficient k_j^r of r result of test j is calculated based on the difference in frequencies of cases when objects of different diagnostic classes have the particular test result. The bigger the probability of assigning object i to different diagnostic classes based on r result of test j , the bigger the value of validity coefficient.

$$k_j^r = \sum_{s_1 \in S} \sum_{s_2 \in S} \left(\frac{N_{s_1} \langle X_i | x_{ij} = r \rangle}{N_{s_1}} - \frac{N_{s_2} \langle X_i | x_{ij} = r \rangle}{N_{s_2}} \right)^2 \quad (13)$$

where $N_s \langle X_i | x_{ij} = r \rangle$ is the number of objects in diagnostic class s whose symptom j takes the value $r_j (x_{ij} = r)$;

N_s is the number of objects in diagnostic class s .

Using validity coefficients of test results k_j^r it is possible to calculate the value of validity degree $\hat{\theta}$ of each diagnosis made by an expert:

$$\hat{\theta}(X_i) = \sum_{j=1}^m \bar{K}_j(x_{ij}) \quad , \quad \text{where } \bar{K}_j(x_{ij}) = k_j^{x_{ij}} \quad (14)$$

Boundary value θ_{bdr} of medical record validity is calculated as arithmetic mean of validity degrees of medical record in the teaching selection.

During computerized diagnostics of object X_0 based on a set of test results software system calculates the validity degree of the given diagnosis θ :

$$\theta(X_0) = \min \left(\frac{\sum_{j=1}^m \bar{K}_j(x_{0j}) \cdot I_j}{\theta_{bdr}}, 1 \right) \quad , \quad \text{where } I_j = \begin{cases} 0, & \text{if } x_{0j} = \emptyset \\ 1, & \text{otherwise} \end{cases} \quad (15)$$

If $\theta(X_0)$ takes the value which is less than 1, that is the sum of integral weight of the obtained test results is less than boundary value θ_{bdr} , the diagnosis is considered to be groundless and computerized system advises on additional checkup of the object.

2.3) Method of the entropy reducing for additional survey

The task of selecting tests for additional checkup of object X_0 is multi-objective extremum problem with the following objective functions [10]:

- maximizing the accuracy of the follow-up diagnosis (using suggested additional tests);
- minimizing the cost of additional tests;
- minimizing the duration of additional tests;
- minimizing the possible damage caused by additional tests.

The most important task of the iteration diagnostic model is maximizing accuracy of the follow-up diagnosis. Put it in other way, it is necessary to select a set of additional tests that will enable sharing of the most currently probable diagnoses in the best way. To evaluate the accuracy of the follow-up diagnosis the notion of information theory entropy [4] will be used. Entropy H in information theory is measure of uncertainty. In the particular case it is measure of diagnosis uncertainty. As the following events «if test j is conducted, the uncertainty is H » are considered, it is required to introduce a concept of conditional entropy $H(X|Y)$.

$$H(X|Y) = \sum_{r=1}^R H(X|Y = r) \cdot P(Y = r) \quad (16)$$

Let A be an event of occurring of an object of some class and A_k – a random event of occurring a class k object. Event of obtaining result r for test j of object X_0 is $B_j^r (j \in M)$. When selecting additional tests it is implied that a subset of tests $T_i = \{1, \dots, t\}$ is

conducted, that is the probabilities that a particular object belongs to different diagnostic classes are known: $P(A_k|B_1^{r_1}, \dots, B_t^{r_t})$. It is required to select the tests providing maximum certainty of the follow-up diagnosis. To do that, it is suggested to select test t^* as an additional test if it reduces in the best possible way the probability distribution entropy $P(A|B_1^{r_1}, \dots, B_t^{r_t}, B_{t^*})$, where B_{t^*} is the event of conducting test t^* . That is it is necessary to minimize the uncertainty of diagnosis based on one additional test t^* . Probability distribution entropy is equal to:

$$H(A|B_1^{r_1}, \dots, B_t^{r_t}, B_{t^*}) = \sum_{r=1}^R H(A|B_1^{r_1}, \dots, B_t^{r_t}, B_{t^*}^r) \cdot P(B_{t^*}^r) \quad (17)$$

When selecting a medical test it is not possible to predict its result in advance, but it is possible to detect the probability of each of the possible outcomes, accordingly:

$$P(B_{t^*}^r) = \sum_{k \in S} P(B_{t^*}^r | A_k) \cdot P(A_k | B_1^{r_1}, \dots, B_t^{r_t}) \quad (18)$$

Using the definition of entropy the value $H(A|B_1^{r_1}, \dots, B_t^{r_t}, B_{t^*}^r)$ is expanded as:

$$\begin{aligned} H(A|B_1^{r_1}, \dots, B_t^{r_t}, B_{t^*}^r) &= \\ &= - \sum_{k \in S} P(A_k | B_1^{r_1}, \dots, B_t^{r_t}, B_{t^*}^r) \cdot \log_2 P(A_k | B_1^{r_1}, \dots, B_t^{r_t}, B_{t^*}^r) \end{aligned} \quad (19)$$

Using the above presented correlations, required additional medical test (or a group of the most suitable tests) T^* is found using:

$$T^* = \operatorname{argmin}_{t^* \in T \setminus T_i} \sum_{r=1}^R H(A|B_1^{r_1}, \dots, B_t^{r_t}, B_{t^*}^r) \cdot P(B_{t^*}^r) \quad (20)$$

C. Software system architecture

In architectural terms the diagnostic system is a collection of three basic components (Fig. 2):

1. Information database of surveys and statistics.
2. Web-service of diagnostics.
3. User interface for diagnostics and working with a survey.

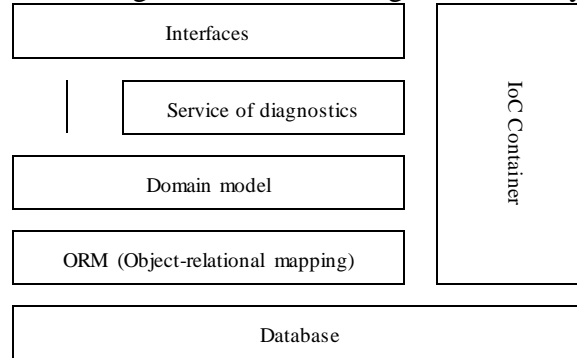


Fig. 2. Architecture of diagnostic system

Information database is a source of data for calculating statistical indicators of teaching selection and storing survey results and technical data as well. Since the

diagnostics web-service has ORM (Object-relational mapping) layer used to construct a Domain model in its internal structure, any relational database management system can be used as an information database, in particular, any product from Microsoft SQL Server family.

Diagnosis web-service is the center of the whole system. Web-service performs both simple and complex tasks: it takes patient's medical record, comes to diagnostic conclusion and produces diagnosis, recommended additional tests and additional service information: explanations of the diagnosis and its probability, etc. Web-service is implemented as a WCF (Windows Communication Foundation) service, running on the IIS (Internet Information Server) web-server. Its implementation is based on modern approaches to programming, that makes it easy to support and expand it. In particular, ORM (Object-relational mapping) technology is applied for constructing Domain model and abstracting from the specific implementation of data storage, widely used dependency injection to ease relations between the components of web-service, pattern Unit of work used to manage secure transactions with data warehouse, etc.

User interface is available in several versions for maximum flexibility of diagnostic service sharing. Currently, personal computer (Desktop) and web interfaces are implemented. Both interfaces are implemented on the platform dotNET 4.0. WinForms technology and MVC 3 application framework were used for desktop interface and for web interface correspondingly. User interface in all implementation is used to input data and get the response from the diagnostic service. In the future, interfaces for mobile platforms, as well as implementation of software extensions integrated into the software systems of medical facilities can be implemented.

III. CONCLUSION

The article describes software system for diagnosing uncertainly defined diseases. Currently, the system has an application for diagnosing children hypermobility syndrome. The diagnostic system is an affordable and simple diagnostic tool that allows diagnosing the disease at an early stage, avoiding it and preventing the development of a large number of secondary diseases. The core of the software system is mathematical methods that can conduct the diagnostics and make the selection of additional medical tests that are required for follow-up diagnosis. Diagnostic information system implements the concept of a diagnostic service, which has a variety of interfaces. This makes it possible for patients without any special training or equipment to use the diagnostic service. It, in turn, greatly simplifies implementation and dissemination of information diagnostic services. Feasibility of developed diagnostic algorithm is proved by the test, performed under the supervision of an expert in children hypermobility syndrome. Testing was performed as follows:

1. HS was diagnosed with method of sampling frequencies on the basis of full survey data.
2. 30 symptoms were randomly selected from the full survey (49 symptoms), their values were assumed to be known, the values of the other 19 symptoms were taken as unknown. Diagnosis was made with iteration diagnostic model with the maximum number of iterations (the number of additional test results are open) below 8.
3. 20 symptoms were randomly selected from the full survey (49 symptoms), their values were assumed to be known, the values of the other 29 symptoms

were taken as unknown. Diagnosis was made with iteration diagnostic model with the maximum number of iterations below 5.

4. An expert selected 15 highly indicant symptoms from the full survey (49 symptoms), their values were assumed to be well known, the values of other 34 symptoms were taken as unknown. Diagnosis was made by an iteration diagnostic model with the maximum number of iterations below 3.

Test results are presented in Table I.

TABLE I
TEST RESULTS

	The 1 st degree	The 2 nd degree	The 3 rd degree	Total
Method of sampling frequencies (49)	88,8%	86,0%	86,9%	87,0%
Iteration model (30+8)	66,7%	78,0%	78,3%	75,0%
Iteration model (20+5)	59,3%	72,0%	69,6%	68,0%
Iteration model (15 +3)	81,5%	84,0%	82,7%	83,0%

Diagnostics with a random set of symptoms decreases diagnostic accuracy in proportion to the number of symptoms involved. However, the most important result of the experiment is that the correctness of diagnosis based on the expert's list of symptoms is similar to the result of diagnosis based on the complete set of symptoms. Since in medical practice doctors rely on a small set of the most indicant symptoms of the disease, it can be concluded that the suggested iteration scheme is quite effective in the diagnosis of medical conditions to be used as a decision support tool.

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